ss(+)RNA Viruses

Introduction

The viruses in this lesson are all single-stranded positive-sense RNA viruses, abbreviated ss(+)RNA. Learning them together in a single lesson will help carve out a spot in your memory, a mental clustering to help you remember which viruses are the ss(+)RNA viruses. Don't learn this family is ss(+)RNA or that family is ss(+)RNA. Learn only that the viruses in this lesson are the ss(+)RNA viruses, and use Figure 4.1 as the advanced organizer. And because all ss(+)RNA viruses share the same microbiology (except coronavirus), you can learn the microbiology for ss(+)RNA viruses once, and apply to all.

ss(+)RNA viruses share structural and replication similarities, as discussed in the next section. Like the DNA viruses, the virology categorization system sees them as similar. However, the diseases they cause are NOT similar. This lesson, like the last, focuses mainly on the diseases they cause, though the lesson is mapped according to virus family, as shown in Figure 4.1, with increasing size from left to right.

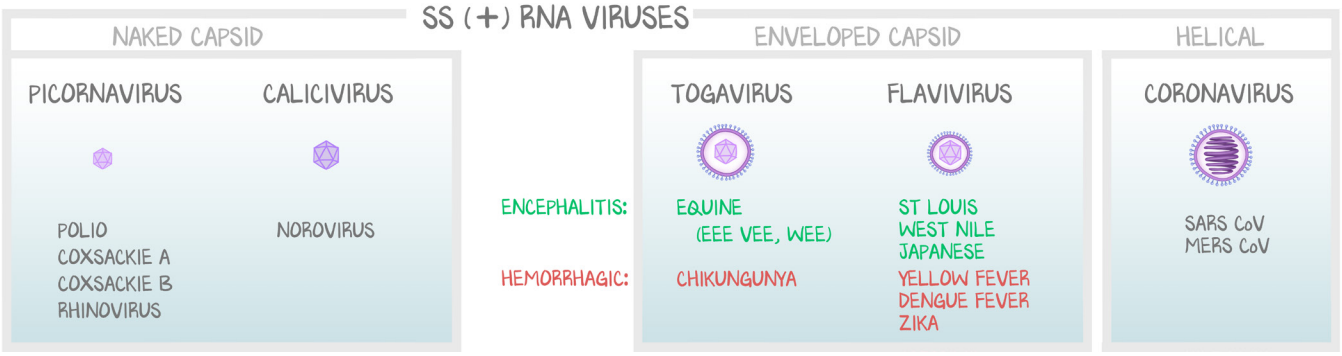

Figure 4.1: Lesson Map
The illustration progresses smallest on the left to largest on the right. Refer back here as you progress through the lesson, putting into perspective the details you are learning.

ss(+)RNA Virus Reminder

We learned from the first two lessons in this Virus series that we can make generalizations about the structure and function of these viruses because they are all ss(+)RNA viruses, thus limiting the amount of detail we'll need to memorize per virus. Here it is again, summarized.

All ss(+)RNA viruses are **single stranded.**
All ss(+)RNA viruses are **icosahedral.**
All ss(+)RNA viruses replicate in the **cytoplasm**.
All ss(+)RNA viruses have a **translatable genome**, and code for RNA-dependent RNA polymerase.
All ss(+)RNA viruses, even those that are enveloped, are **cytolytic** (except hepatitis C).
Flavi and Toga are **enveloped**; the rest are not.
"Flavi and Toga" is the intentional abbreviation and conjoining of Flavivirus and Togavirus, and should be considered one virus family.

Coronavirus is the exception—it is helical, and being helical must also be enveloped.

From here on, we go virus by virus. We aren't going to say, "single stranded, icosahedral, cytoplasm, codes for RdRp," for every virus. You can assume that these attributes apply to all the viruses that follow, unless exceptions are called out.

Picornaviruses

The name of the virus family tells you about its structure and size. It is **small** (pico-), made of **RNA** (-rna-), and is a **virus** (-virus). This is one of the most frustrating families to study. It has several subclassifications, which in turn have viruses that cause various diseases. There are over 230 members in this family. You need to know five. All picornaviruses share the fact that their **genome is mRNA**. More than just positive-sense, more than can-be-read-by-a-ribosome, the genome is translated without interruption into a **polyprotein** which is then cleft into enzymatic and structural proteins. It has a poly-A tail on the 3' end, and a viral-protein equivalent to a 5'-methylguanine cap on the 5' end, just like human mRNA. Ribosomes start at one end and translate continuously until the stop signal. There is only one start point and one end point, just like human mRNA. Part of that genome codes for an **RNA-dependent RNA polymerase**. All picornaviruses are **naked** viruses, and so cannot bring enzymes or transcription factors with them when they infect.

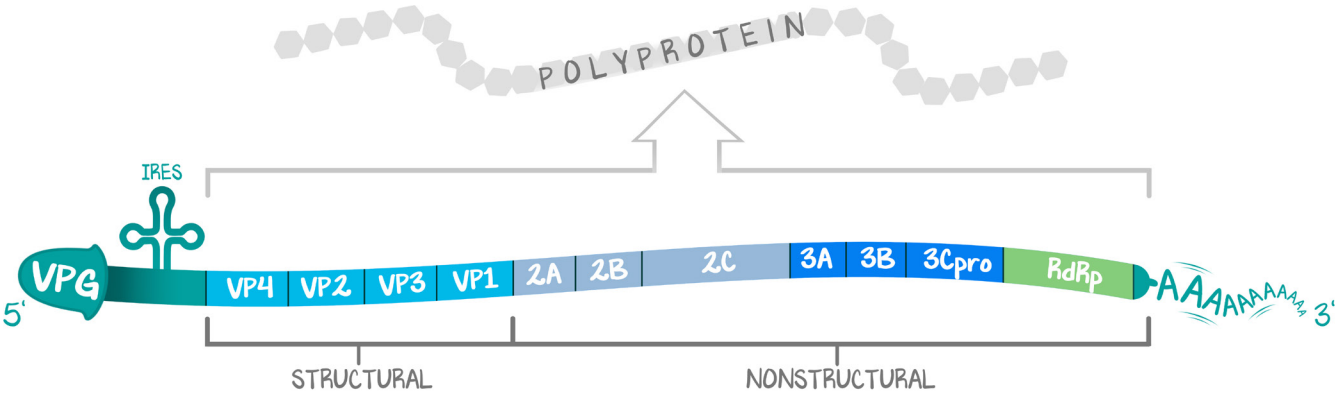

Figure 4.2: Picornaviruses Are mRNA
The 5' VPg resembles the host cell's 5'-methylguanine cap, the viral 3'poly-A tail is identical to the host cell's 3' poly-A tail, and the RNA genome is contiguous. The contiguous RNA genome, when translated by ribosomes, produces a contiguous polyprotein. Post-translational modification of that polyprotein amino acid sequence results in multiple viral proteins.

Every virus in the *Picornaviridae* family is mRNA; is made into a polyprotein, then cleaved up; is ss(+)RNA, icosahedral, and naked; and causes lysis during its replication cycle. Some picornaviruses are **resistant to harsh environmental conditions** (sewage, gastric pH), which facilitates their transmission via the **fecal-oral route**. These viruses are **enteroviruses** (entero means "gut," the enterocyte is the cell that lines the epithelium of the gut lumen). Enteroviruses are polio, Coxsackie A, and Coxsackie B. The only non-enterovirus picornavirus we will study is rhinovirus.

Hepatitis A is also a picornavirus. It is also an enterovirus with tropism for the liver. We discuss it in Viruses #7: *Hepatitis Viruses*.

Picornaviruses That Are Enteroviruses

Since 1967, numerical nomenclature has been used to distinguish between newly isolated enteroviruses. Before science figured out what was causing the diseases we knew existed, we named things poorly. We want you learning that there is a poliovirus, a Coxsackie A virus, and a Coxsackie B virus, each of which is associated with a specific disease. That isn't how things are actually categorized (there are multiples serotypes of each), but the system we propose works when considering a clinical perspective. The overlap of clinical syndromes across the enteroviruses is frustrating because it is your job to be able to separate them. Virologists will say that all enteroviruses can cause disease in any organ. What we're going to do is discuss the common syndromes but then identify key disease-virus pairs that you should associate as exclusive. You are not supposed to be a virologist, you are supposed to be able to practice medicine.

All enteroviruses are ingested, fecal-oral route. All enteroviruses replicate in the oropharynx. This causes a sore throat for a few days after inoculation. All enteroviruses then get into the blood (**viremia**). If there are antibodies to the virus, the virus is stopped right then and there, and no chance of symptoms arises. If no antibodies exist, viremia results in the general viral symptoms of fever, malaise, and a headache for about a week. Going viremic means the virus has access to all tissues. Individual viruses have tropism for particular organs. We are going to teach you a grossly oversimplified approach to these enteroviruses. For you, there is a one-virus/one-syndrome pair, without overlap. The name microbiology has given the virus, we give to the syndrome the virus causes. For example, all serotypes of Coxsackie A (virology) cause the syndrome Coxsackie A (OnlineMedEd), which is herpangina or hand-foot-mouth disease. This will make more sense when you see it in action.

The **most common presentation** of any enterovirus infection is **asymptomatic**. Exposure to the virus means antibodies develop, and these antibodies offer permanent immunity. The vast majority of the symptomatic cases are mild, and the patient may not even recognize they had an infection at all. Only a very small percent suffer the overt clinical syndromes we are going to discuss next. There is one common link between them all. All enteroviruses can cause infection of the **brain**. If the virus gets in the brain, the presentation is usually an **aseptic encephalitis**—fever, headache, and malaise—that self-resolves. Aseptic means "not bacterial meningitis" and "no bacteria grows on culture." Because all enteroviruses can affect the brain, all enteroviruses can cause a polio-like paralytic syndrome. But because it is literally called polio-like, we're going to give that syndrome to polio, rather than count it as a commonality between them. Figure 4.2 shows a simplified predilection, virus to tissue to disease.

What we want you learning is that all enteroviruses cause sore throat and fever, and can get into the brain. Individual enteroviruses express specific tropism to specific organs, resulting in specific syndromes. Polio goes to the spinal cord and causes paralysis, Coxsackie A goes to the skin and causes vesicles, and Coxsackie B goes to striated muscle and causes inflammation. *(Hepatitis A is also an enterovirus with tropism for the liver, discussed in Viruses #7.)* The name "Coxsackie" is for the city in New York where the first Coxsackie virus was discovered. All Coxsackie viruses are picornaviruses and are also enteroviruses. However, the diseases they cause have little overlap, despite their names being so similar.

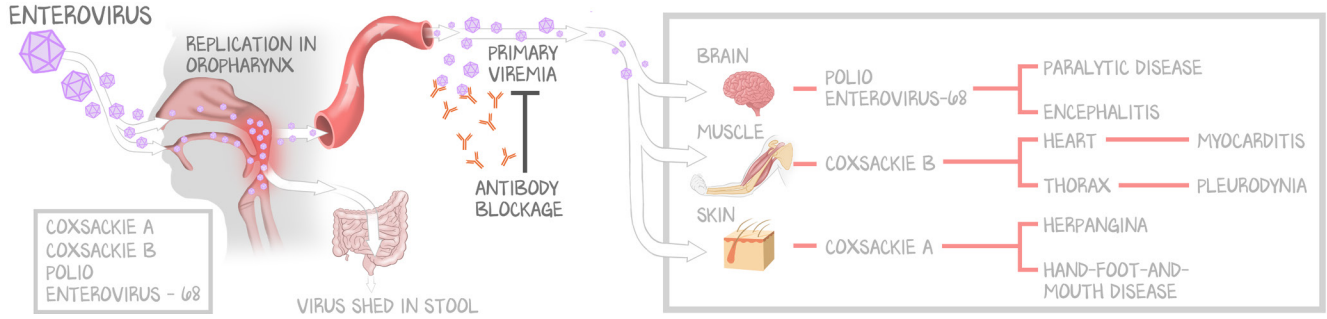

Figure 4.3: Enterovirus Pathogenesis
All enteroviruses enter the oropharynx and replicate. If no antibodies are present, primary viremia allows the virus access to the body. Poliovirus and enterovirus 68 have a predilection for the brain and cause paralytic disease. Coxsackie B has a predilection for striated muscle and can cause myocarditis or pleurodynia. Coxsackie A affects stratified squamous epithelium, causing mucosal herpangina and cutaneous hand-foot-mouth disease.

Poliovirus causes **paralytic poliomyelitis** because polio goes to the brain and spinal cord. Approximately 90% of those infected with polio have no symptoms, 5% develop a nonspecific febrile illness, 5% have a nonparalytic aseptic meningitis, and < 1% of patients infected with polio get paralytic polio disease. **Paralytic polio** is the result of a **cytolytic infection** of **motor neurons** in the anterior horn of the spinal cord, cytolytic infections of the lower motor neurons. Loss of lower motor

neurons results in the loss of the final "go" signal to skeletal muscle, presenting with **flaccid paralysis** and **decreased reflexes.** Motor neurons are variably affected, meaning that any skeletal muscle can be affected, and the effects are asymmetric. All sensation is maintained. Antibody immunity develops and clears the infection in all cases. Antibody immunity is lifelong after the infection. However, motor neuron death is permanent. Because polio is a worldwide disease, even if as few as 0.1% were affected, 0.1% of everyone on the planet is still a big number. And even though the infection is short-lived, the morbidity of paralysis is lifelong. **Postpolio syndrome** is seen later in life (30–40 years later) and causes further deterioration of the originally infected muscles. Better to have those antibodies before you get exposed, and escape the disease altogether. There are **two vaccines**. The **oral polio vaccine** (OPV) was invented by Albert Sabin, and is known as the Sabin vaccine. It is a **live attenuated vaccine** which is ingested orally—just like poliovirus is ingested. Because it is live attenuated, the vaccine induces a robust immunogenic response. Only **one dose** is needed to confer lifelong immunity. Being given orally means it can be administered by anyone, not just trained medical professionals. Easy to administer and only one dose required make the oral vaccine the method of choice to vaccinate impoverished Third World countries. The drawback to the oral vaccine is that it **can cause paralytic poliomyelitis**, and a person who is developing antibodies may shed virus and infect others without knowing. To be the one person from the community being vaccinated who gets paralytic polio sucks just as much for that person as it would have if they got polio without the vaccine. The massive reduction in total number of polio cases, the benefit to society and the community, offsets the negative of that one person's misery. The second vaccine is the **inactivated polio vaccine** (IPV) or Salk vaccine, developed by Jonas Salk. The IPV is administered **intramuscularly**. Being intramuscular and inactivated, the immunogenic response is much less than OPV, and **booster shots** are required to achieve immunity (three shots total). Because it is not ingested and not alive, there is no risk of paralytic poliomyelitis and no shedding of virus with IPV. But it does require access to health care, and trained professionals to administer. Thus, the **IPV** is the **vaccine method of choice in the US**. Poliovirus has subtypes, all of which cause polio. Poliovirus is a subtype of enterovirus. Enterovirus 68 is a subtype of enterovirus. Enterovirus 68 is effectively another poliovirus subtype, but has been cataloged the right way, as enterovirus 68, not poliovirus 12.

Coxsackie A goes to the skin, causing hand-foot-mouth disease—that's the association we want sticking. Coxsackie A can also go to just the mouth and throat, causing herpangina. Coxsackie A causes an eruption of vesicles on an erythematous base. That may sound familiar. Herpes simplex virus lesions were described the same way, and herpes simplex virus commonly causes oropharyngeal lesions. "Herpangina" was so named because the lesions looked like herpes lesions ("herpes" of herp-angina) and because they cause chest pain ("angina" of herp-angina). They cause chest pain because they occur in the esophagus, but do not cause myocardial ischemic chest pain (which is how we now use the word angina). **Herpangina** is characterized by fever, sore throat, and odynophagia, and has vesicles on an erythematous base on the pharynx. Again, sounds like it could be HSV. But if sampled, there would be no intranuclear inclusions, and HSV PCR would be negative, meaning it is not HSV. **Hand-foot-mouth disease** is characterized by fever and vesicles on an erythematous base which occur on the hands, feet, and mouth. It is always bilateral and fairly symmetric. HSV does not go to the palms and soles (unless some very specific and elaborate sex practice intentionally infected only these areas of skin). In both cases, Coxsackie A infections are **self-limiting** acute cytolytic infections, do not establish a latent infection, and therefore do not recur. That also means that treatment with antiviral medication is not required or even recommended. Lifelong immunity follows infection. If you think it's HSV, but is confirmed to be not HSV by laboratory diagnostics, it is probably Coxsackie A. There is no treatment and no vaccine for Coxsackie A.

Coxsackie B goes to striated muscle. When that striated muscle is heart muscle, it causes myocarditis. When that striated muscle is skeletal muscle, it causes pleurodynia. **Pleurodynia** is an acute illness with fever and unilateral **pleuritic chest pain** accompanying exquisitely tender skeletal muscles. It is

self-limiting and lasts for 4 days. Labs may reveal an elevated creatine kinase, the blood test for muscle inflammation. **Myocarditis**, inflammation of the heart muscle (myocardium), from Coxsackie B presents with fever, chest pain, elevated troponins, but no ischemic changes on EKG and, if performed, would have clean coronaries. For adults, it is usually self-limiting without sequelae. Myocarditis-induced heart failure can occur in any patient, but those most vulnerable are neonates. Neonates who are born healthy without birth defect, then become febrile and develop **new onset heart failure**, have likely suffered from Coxsackie B. There is no treatment and no vaccine.

Picornavirus Not Enterovirus = Rhinovirus

Rhinovirus is a picornavirus but is **unable to replicate in the gastrointestinal tract**. Rhinovirus cannot withstand the gastric pH. Rhinoviruses **grow best at 33°C**; any warmer and they don't do well. Humans are 37°C. That means rhinoviruses won't be causing any visceral or cerebral diseases. Rhinovirus is the predominant cause of the **common cold**. It is spread by **respiratory droplets** or on fomites (hands or contaminated objects). It affects the nasal epithelium, resulting in rhinitis, congestion, sneezing, headache, and a minor pharyngitis. It is usually self-diagnosed, is always self-limiting, has no vaccine, no treatment, and no sequelae. Because growth at hot temperature is difficult, hot chicken-noodle soup might actually work (inhaling the steam from the soup helps kill the virus). Because there are so many serotypes of rhinovirus, it is not a good candidate for a vaccine—the only thing common about the "common cold," is the symptoms.

Norovirus

Norovirus is the most common cause of foodborne disease outbreaks in the United States. It causes **acute watery diarrhea**. It is part of the *Caliciviridae* ("*Dracarys!*" . . . just kidding, not that Khaleesi) family, all of which also cause diarrhea. The only virus that matters is norovirus. Norwalk virus, the prototypical norovirus, was discovered in Norwalk, Ohio. These terms, Norwalk virus and norovirus, are used interchangeably. Norovirus genome is contained in a **naked capsid**. Its genome is positive-sense and has a 3' poly-A tail and viral-protein equivalent of the 5' methylguanine cap, similar to picornavirus. Norovirus is spread **fecal-oral**. Norovirus is one of the main reasons why all employees must wash their hands when leaving the bathroom. Because it is naked, it is resistant to environmental pressure—detergents, drying, and acid do little to it. While food handlers contaminating food would cause disease, because Norwalk virus survives so well outside of a human host, if anyone puts norovirus down on any surface, anyone else can pick it up from that surface. Suspect norovirus when **many people simultaneously** get an acute gastroenteritis. This is classically associated with **cruise ships** on the boards. The disease is always self-limiting (48–72 hours). There is no treatment, no vaccine, and no sequelae.

Arboviruses

The togaviruses and flaviviruses should be learned as the **arboviruses** (arthropod-borne viruses). The next paragraph is painful to read. We include it so you know that we are intentionally taking a huge shortcut around viral taxonomy. We're going to treat this section as arbovirus, and not the technical correct virology way of doing it.

Technically, the *Alphavirus* genus of the *Togavirus* family comprises the *Togavirus* arboviruses, which share similarities with the *Flavivirus* family arboviruses. The *Rubivirus* genus of the *Togavirus* family does not share those similarities, and causes rubella, the German measles. The hepaciviridae are flavivirus that cause hepatitis C (hepa-c-iviridae), and are not arboviruses. Wow, is that painful to follow. What we want you learning is, "*Toga and Flavi are arboviruses*," and, separately, "*Rubella causes German measles; hep C virus causes chronic hepatitis*."

Toga and flavi are **enveloped**. They enter the cell via fusion of the membrane. Flavi has a continuous mRNA that makes a polyprotein (like picornavirus and norovirus); toga has early and late proteins. All arboviruses are **cytolytic** and cause only acute disease. Even though they are enveloped, their assembly and release leads to lysis.

Togavirus arboviruses are the **equine encephalitis** viruses (Eastern equine encephalitis, Western equine encephalitis, Venezuelan equine encephalitis) and **chikungunya**. *Flavivirus* arboviruses are the **other encephalitis** viruses (St. Louis, West Nile, Japanese) and the **hemorrhagic diseases** (yellow fever, dengue, and Zika). All arboviruses are carried in a vector: **mosquitos**. A viremic human is bitten by a mosquito, who holds onto the virus for another human. The generous insect feeds off another, uninfected human and delivers the virus to that uninfected human. The patient is then viremic. Each arbovirus exhibits tropism for a particular tissue. Where the virus goes determines the symptoms. We've further simplified arboviruses into two categories. Those that have tropism for the brain cause encephalitis (**encephalitis arboviruses**). Those that have tropism for not-the-brain cause hemorrhagic disease and pain (**hemorrhagic arboviruses**).

ENDEMIC TO	ENCEPHALITIS	FAMILY	HEMORRHAGIC	ENDEMIC TO
United States	West Nile	Flavi	Yellow fever	Africa and S. America
China	Japanese		Dengue fever	Tropical, Caribbean
			Zika	Caribbean
North America	Eastern equine	Toga	Chikungunya	Caribbean, West Africa
North America	Western equine			
South America	Venezuelan equine			

Table 4.1: Arboviruses

The **encephalitis diseases** present with . . . get ready for it . . . encephalitis. Arboviruses cause **viral encephalitis** that is the not-HSV viral encephalitis. Encephalitis presents with fever, headache, and altered mental status. A lumbar puncture is performed that reveals that the diagnosis is not bacterial meningitis (there are not 1,000s of neutrophils) and the diagnosis is not HSV encephalitis. That leaves us with the diagnosis of "aseptic meningitis" or "I- don't-know-encephalitis." The thing is, at this point, having ruled out bacterial meningitis and HSV encephalitis, it doesn't matter what the diagnosis is—whether it is viral, arbovirus, or any other etiology, **the management is supportive care only.** Arbovirus encephalitis cannot be treated, and must simply run its course. Knowing which arbovirus it is doesn't matter. Knowing that it is even related to mosquitos doesn't matter. Arbovirus encephalitis cannot be treated, and must simply run its course. Most patients infected with an encephalitis virus never know they have it; most cases are asymptomatic.

In 2016 the CDC recorded a grand total of 2,160 arbovirus infections. West Nile virus was the cause of 2,150 of them, and half of those were neuroinvasive (encephalitis, meningitis, or flaccid paralysis). West Nile also presents with a flaccid paralysis. What you should take away from this is that **West Nile is the one to know**. So what we want you taking away from this is that **West Nile** is the **most common arbovirus** infection, is most likely to cause neuroinvasive disease, and **causes flaccid paralysis**. Once thought to be similar to Guillain-Barré syndrome, causing demyelination, it is now believed that the flaccid paralysis results from more of a poliomyelitis-like process, with death of anterior horn neurons. If the patient lives, the symptoms of encephalitis resolve on their own; the weakness does not. Although

West Nile encephalitis is named for a river in Africa, its highest prevalence is in the US and Canada (the United States is technically west of the Nile).

The other ones do not matter. St. Louis virus was diagnosed eight times—that's so few times that proper written communication calls for spelling the number. Japanese encephalitis is common in Japan. All of the equine viruses (Western, Eastern, Venezuelan) are associated with horses. Killed-virus vaccines are available against Eastern equine, Western equine, and Japanese encephalitis.

Soapbox:

If you order an arbovirus panel on a patient with viral meningitis, and the test is positive, you must report it to the CDC. When the CDC receives word of an arbovirus infection, it posts a notice about it. Other medical providers see the posting, and are therefore more likely to test the CSF of patients with encephalitis. More tests come back positive, and more reporting to the CDC occurs, generating more postings and media coverage. More medical providers order more arbovirus testing on the CSF of their patients. Whew! An EPIDEMIC of arbovirus infections! No . . . it is an epidemic of physicians ordering tests they shouldn't have ordered. Because you know what benefit all those patients who tested positive for arbovirus got from that positive test? Nothing. Because no one's management changed. Before the test it was supportive care. After the test it was supportive care. Don't order tests you don't need. Don't order tests where your management will be the same regardless of the outcome of the test.

Figure 4.4: Dustyn's Soapbox

The **hemorrhagic diseases** present not with encephalitis, but with either hemorrhage, hepatitis, or pain. This is another oversimplification. Dengue and yellow fever can present with hemorrhagic fever, but do not always present with hemorrhage. When there is no hemorrhage, there is a lot of pain. Since Zika and Chikungunya also cause pain, and all four viruses are so low-yield to United States medicine, we've lumped Zika and Chikungunya into "hemorrhagic disease," making dengue, yellow fever, Zika, and Chikungunya the non-encephalitis-viruses-you-get-outside-the-country. We thought "hemorrhagic diseases" sounded better.

Dengue fever hurts like hell, nicknamed **breakbone fever**. It presents with a high fever, rash, and bone pain that lasts a week. It is endemic to the tropical areas and will be seen in the United States in someone returning from an endemic area. There are four serotypes of dengue fever. Exposure to one confers immunity only to that one. Exposure to another serotype of dengue results in **immune enhancement**—the immune system is able to contain the virus faster and better. But it does that by killing infected cells, which means that instead of immunity avoiding infection, you get a more severe presentation because of that immunity. Getting dengue twice (but from different serotypes) results in **dengue hemorrhagic fever** (normal painful dengue, plus spontaneous internal bleeding). If the bleeding gets bad enough, the hemorrhagic fever progresses to **dengue shock syndrome** (spontaneous internal bleeding of large volume). Dengue hurts the first time you get it, hurts and bleeds the next time you get it. A vaccine against all four strains is in the works. Making a vaccine against anything less than all four strains will prevent the initial breakbone fever, but also prime every recipient for dengue hemorrhagic fever on their first presentation.

Yellow fever is endemic to Africa and South America. This is a severely fatal disease—50% mortality. A mosquito injects the virus into the bloodstream, where it enters the Kupffer cells of the liver. Hepatocellular injury impairs processing of bilirubin, which accumulates, causing jaundice, a yellowing of the skin and eyes for which the disease is named. Yellow fever can also cause **gastrointestinal bleeding**, leading to shock. There is no treatment, but there is a **great live attenuated vaccine**. Anyone traveling to an endemic area must be immunized. While dengue bleeds the second time you get it, yellow fever bleeds the first time you get it. And if you get it, chances are there won't be second time (because you die). **Vaccinate** anyone traveling to endemic areas. This DOES have clinical value in the way of travel medicine and your own personal knowledge, should you do medical mission trips to endemic areas.

Zika has gained much attention because of the birth defects that are possible when a pregnant woman contracts the virus. While Zika can present with dengue-like symptoms (**it hurts**), most of the time the patient is asymptomatic, meaning a pregnant mother does not know she has contracted the virus and given it to her fetus. Zika is endemic to the Caribbean. The only real thing you need to know about Zika is that women planning to get pregnant or who are pregnant should avoid endemic areas (or go to endemic areas while young and not planning to have kids, so she becomes immune).

Chikungunya means, "the illness of the bended walker," referring to the **crippling arthralgias** associated with infection. Chikungunya hurts, but generally leaves no lasting sequelae. It was formerly a West African disease, though has seen a resurgence in the Caribbean and Central America because of a return of its mosquito vector.

The names of the mosquito vectors are excluded. Do not memorize mosquito vectors for viruses. The *Anopheles* mosquito carries malaria. That is the only mosquito species you should know.

Coronavirus

Coronavirus (CoV) is the exception to the ss(+)RNA commonalities, and is the only one with a **helical** nucleocapsid. Because it is helical, and helical nucleocapsids cannot exist without an envelope, coronavirus is an **enveloped** virus. It is the largest of the ss(+)RNA viruses. **Coronavirus** used to be **"the other rhinovirus."** Indeed, most coronavirus strains do nothing more than cause the nuisance symptoms of the common cold. These CoV strains are the next most common cause of cold symptoms after rhinovirus. Most coronaviruses grow optimally at 33–35°C, like rhinovirus. Most coronaviruses are shed from infected humans in form of aerosols. Those aerosols are projected at another human (sneezing, coughing), who gets infected, just like rhinovirus.

However, the outbreak of Severe Acute Respiratory Syndrome (SARS-CoV, Asia) and then later Middle Eastern Respiratory Syndrome (MERS-CoV, Arabian Peninsula) revealed to medicine coronaviruses that optimally grew at human temperature and were much more deadly. These coronaviruses **grow at 37°C**, cause **severe pulmonary disease**, and are transmitted **from animals to humans** (zoonoses) as well as human to human. SARS-CoV causes an atypical pneumonia with fevers and myalgias. Patients with preexisting pulmonary disease are affected the most, and likely account for the high 10% mortality. The virus jumps from animals raised for food (civets, raccoon dogs, ferret badgers) to humans. MERS-CoV is carried by bats and camels and causes an even more severe respiratory distress syndrome, with near 50% mortality. Almost all cases of MERS-CoV have occurred in the Arabian Peninsula.

Enteroviruses	Poliovirus	Picornavirus and Enterovirus Inoculation, 3 days of sore throat, one week of fever Infects anterior horn neurons, results in flaccid paralysis Oral vaccine—easy to give, one dose required, can cause disease IM vaccine—hard to give, multiple doses required, safe	
	Coxsackie A	Picornavirus and Enterovirus Inoculation, 3 days of sore throat, one week of fever Infects skin, causes hand-foot-mouth disease (and herpangina)	
	Coxsackie B	Picornavirus and Enterovirus Inoculation, 3 days of sore throat, one week of fever Infects cardiac muscle, causes myocarditis, CHF in neonates	
Encephalitis arboviruses	St. Louis	Flavi	Seven cases diagnosed in 2016. It is a distractor
	West Nile	Flavi	Most common arbovirus in United States Most likely to be neuroinvasive (cause encephalitis) Presents with flaccid paralysis
	Japanese	Flavi	Japan, has vaccine
	Eastern equine	Toga	Horses, has vaccine for the horses
	Western equine	Toga	Horses
	Venezuelan equine	Toga	Venezuela
Hemorrhagic Arboviruses	Yellow fever	Flavi	Vaccinate travelers to endemic areas (South America, Africa) 50% mortality if contracted Liver failure (bilirubin turns you yellow), death from GI bleed
	Dengue fever	Flavi	Endemic to Caribbean 1st exposure: Breakbone fever, extreme pain and fever 2nd exposure: Immune enhancement, looks like yellow fever
	Zika	Flavi	Endemic to Caribbean Causes pain syndrome (but usually asymptomatic) Teratogenic, avoid travel to endemic areas
	Chikungunya	Toga	Endemic to Caribbean Pain syndrome, distractor for dengue
Shmeh viruses	Rhinovirus	Picornavirus not enterovirus Cannot grow at 37°C, only at 33°C Causes common cold symptoms	
	Coronavirus-CoV	Cannot grow at 37°C, only at 33°C, so is the other rhinovirus SARS-CoV = China, host shift from small mammals, grows at 37°C MERS-COV = Arabian Peninsula, host shift camels, grows at 37°C	
	Norovirus	Cruise ship diarrhea Self-limiting watery diarrhea, 48 hours in duration	

Table 4.2: Summary of Enteroviruses
Enteroviruses cause enteric symptoms, then viremia permits additional symptoms based on viral tropism. Arboviruses are divided into those that cause encephalitis (only West Nile matters), and not-encephalitis (hemorrhagic). Shmeh viruses cause mild disease that is self-limiting, and has no treatment, vaccine, or sequelae.